Stroke in Latin America

Burden of Disease and Opportunities for Prevention

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ABSTRACT

The epidemiological transition in Latin America toward older urban dwelling adults has led to the rise in cardiovascular risk factors and an increase in morbidity and mortality rates related to both stroke and myocardial infarction. As a result, there is an immediate need for effective actions resulting in better detection and control of cardiovascular risk factors that will ultimately reduce cardiovascular disease burden. Data from case-control studies have identified the following risk factors associated with stroke: hypertension; smoking; abdominal obesity; diet; physical activity; diabetes; alcohol intake; psychosocial factors; cardiac causes; and dyslipidemia. In addition to its high mortality, patients who survive after a stroke present quite frequently with marked physical and functional disability. Because stroke is the leading cause of death in most Latin American countries and also because it is a clearly preventable cause of death and disability, simple, affordable, and efficient strategies must be urgently implemented in Latin America.

Latin America comprises an area of 21,069,500 km^2 (7,880,000 square miles), containing widely different environments and consisting of many complex and heterogeneous ethnicities, societies, and cultures. As of 2010, the Latin American population was estimated at >590,000,000 in 20 countries and its combined gross domestic product at 5.16 trillion United States dollars (2012), with life expectancy varying from 62 years in Haiti to 79 years in Chile (2011), and the Human Development Index ranging from 0.456 in Haiti to 0.819 in Chile (2011) [1].

Marked human and societal development has occurred in Latin America during the last decades. The population is thereby getting better access to education, water and sanitation services, primary health care, cost-effective technologies, and immunizations, as well as benefiting from sustained progress toward preventing and controlling numerous communicable diseases in several Latin American countries [2]. Additionally, life expectancy at birth has recently increased by an average of 6 years, and the incidence of infant mortality has decreased by one-half [1].

Currently, Latin America faces 3 major demographic shifts: 1) population growth, which has slowed; 2) urbanization (almost 90% of the population now live in urban areas); and 3) aging (the ratio of productive adults to elderly individuals is steadily shrinking) [2].

The observed epidemiological transition in Latin America toward older urban dwelling adults has led to a rise in cardiovascular risk factors and an increase in morbidity and mortality rates related to both stroke and myocardial infarction [3].

The Global Burden of Disease study described that in 2005, 87% of worldwide stroke deaths occurred in low- and middle-income countries [4]. From 1970 to 2010, global male life expectancy at birth increased from 56.4 to 67.5 years and global female life expectancy at birth increased from 61.2 to 73.3 years. Male life expectancy at birth rose by 11 years from 1970 to 2010 and by 13 years in females, globally. In Latin America, from 1970 to 2010, male life expectancy at birth increased from 50.5 to 73.9 years and female life expectancy from 56.5 to 77.0 years in Andean Latin America (Bolivia, Ecuador, and Peru); from 60.6 to 71.7 years (males) and from 65.8 to 78.2 years (females) in Central Latin America; from 62.3 to 73.3 years (males) and from 69.5 to 79.9 years (females) in Southern Latin America (Argentina, Uruguay, and Chile); and from 57.8 to 70.5 years (males) and 64.9 to 77.7 years (females) in Brazil. Global life expectancy has increased continuously and substantially in the past 40 years, and this increase has been driven by large declines (≥60%) in child mortality, declines of 40% or more in adult female mortality, and declines of 15% to 35% for adult male mortality, depending on age group [5].

Stroke collectively killed 12.9 million people in 2010, which is 1 in 4 deaths worldwide compared with 1 in 5 in 1990. Ischemic heart disease, stroke, chronic obstructive pulmonary disease, lower respiratory infections, lung cancer, and human immunodeficiency virus/acquired immunodeficiency virus were the leading causes of death in 2010 [6]. There is a consistent reduction in the age-standardized death rate (per 100,000) for those with ischemic stroke (26.6%), hemorrhagic stroke (22.7%), and cardiovascular and circulatory disease (21.2%), although

The authors report no relationships that could be construed as a conflict of interest.
Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.gheart.2014.01.006.

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GLOBAL HEART

VOL. 10, NO. 4, 2015
ISSN 2211-8160
http://dx.doi.org/10.1016/j.gheart.2014.01.006

there is an increase of 89.6% in atrial fibrillation and flutter. In some Latin American countries, ischemic heart disease and stroke are ranked as the 2 leading causes of death [7].

The main objective of the current review is to collectively describe the available scientific evidence associated with the burden of stroke in Latin America to better understand how to prevent and improve outcomes related to stroke in the region along with the need for future research that could be translated into better populationwide cardiovascular health.

EPIDEMIOLOGY OF STROKE IN LATIN AMERICA

In a recent review, Garritano et al. [8] analyzed the mortality trends due to stroke in Brazil from 2000 to 2009. They found a rise in the incidence of deaths until 2006, after which the trend fell until 2009. Data from the Universal Coverage System, in Brazil, show that 97,557 patients died due to stroke in Brazil in 2009. The standard mortality rate for stroke was 115.51 per 100,000 persons, lower than in 2000 when it was 135.88 per 100,000 persons, suggesting a decrease of about 15%. The reduction was seen in both sexes, with reduction of 15% in men and 17% in women [8] (Fig. 1).

In the last decade, well-conducted population-based studies of incidence of stroke have been done in specific Latin American countries. The first was conducted in 2000 in Iquique, Chile. Similarly, additional experience was obtained from Brazil and Mexico. A comparative analysis shows that the crude annual incidence of first-ever stroke vary among these studies from 73.6 and 76.9 (per 100,000), in Iquique (Chile) [9] and Joinville (Brazil) [10], respectively, to 96.1 and 108.0, in Durango (Mexico) [11] and Matão (Brazil) [12], respectively. Table 1 depicts an age-standardized stroke incidence rates from these 4 prospective community-based Latin American studies.

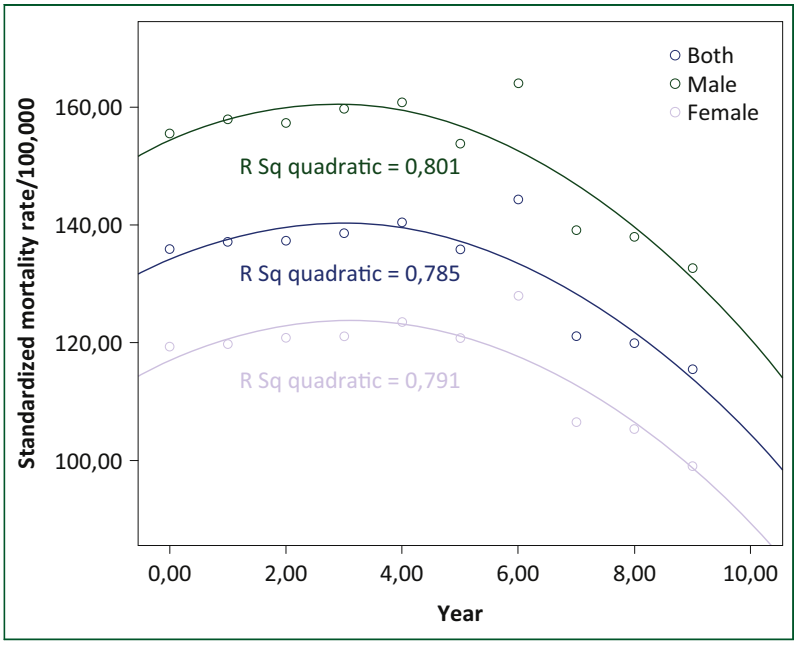

FIGURE 1. Regression of standard mortality rate for stroke trend per 100,000 persons by sex (2000 to 2009) in Brazil.

There are few stroke prevalence studies conducted in Latin America, and those available in the literature have used different methodologies. Due to the discrepancy of data among studies, a valid comparison including age-standardized prevalence data among Latin American countries is not scientifically appropriate to be provided. Despite the lack of such data, those studies convey actual information about the burden of prevalence stroke in those communities.

Abe et al. [13,14] evaluated the prevalence of stroke in a low socioeconomic status population in the city of São Paulo [13]. Of the 4,496 individuals over 35 years old living in the area, 243 initially screened positive for stroke. The age-adjusted prevalence rate for men was 4.6% (95% confidence interval [CI]: 3.5 to 5.7) and for women, was 6.5% (95% CI: 5.5 to 7.5) [14].

In Bolivia, a door-to-door survey was completed in 1994 within the rural areas of the Cordillera Province, Santa Cruz Department. The survey screened 9,955 subjects in 55 communities (with <600 inhabitants) and 16 stroke survivors were identified, indicating that the crude prevalence of stroke was 174 per 100,000 (322 per 100,000 age-adjusted to the world standard population) and 663 per 100,000 in subjects ages ≥35 years. The stroke prevalence was >2-fold higher in men than in women (247 per 100,000 and 99 per 100,000, respectively) and increased rapidly with age [15].

In Argentina, another study of the prevalence of cerebrovascular disease was conducted in Junín. Systematic sampling was used and 5,648 households were evaluated. In 1991, 148 subjects with stroke were identified. The point prevalence ratio was 868.1 cases per 100,000 inhabitants in the total population (473.4 per 100,000 age-adjusted to the worldwide population) and 1,867.4 in those patients of 40 years of age or older (1,534.4 per 100,000 age-adjusted to the worldwide population) [16].

STROKE SUBTYPES AND LETHALITY

Adequate and proper knowledge of the incidence of each of the 3 more common subtypes of stroke, are substantially important, because the support of care in the acute phase is different and also because they have differences in lethality rates. Table 2 summarizes data from 4 population-based studies on the stroke incidence rates by subtype and their respective lethality in Latin America. As observed worldwide, the subtype ischemic stroke has the highest incidence.

RISK FACTORS ASSOCIATED WITH STROKE

There are few reports describing the relationship between cardiovascular risk factors and stroke in Latin America.

TABLE 1. Annual first-ever stroke incidence rates per 100,000 standardized by age in Latin America

Total Population, by Age, yrs	Iquique, Chile, 2000 [9] Incidence rate (95% CI)	Matão, Brazil, 2004 [12] Incidence rate (95% CI)	Joinville, Brazil, 2005–2006 [10] Incidence rate (95% CI)	Durango, Mexico, 2008 [11] Incidence rate (95% CI)
0–24	4.5 (1.9–8.8)		NA	NA
25–34	6.0 (1.6–15.4)	7 (1.9–17.5)*	9.2 (5.3–15.0)	6.3 (2.8–15.2)
35–44	22.5 (12.3–37.7)		26.8 (19.2–36.4)	29.7 (14.6–38.8)
45–54	99.6 (72.1–134.1)	116 (53.2–220.8)	123.0 (102.1–146.9)	64.7 (45.2–92.5)
55–64	308.2 (241.6–387.6)	581 (379.9–850.2)	310.4 (263.3–363.5)	150.4 (111.1–203.5)
65–74	462.5 (356.2–590.6)	895 (585.5–1,308.7)	523.9 (448.5–608.3)	306.3 (233.4–402.0)
75–84	1,036.7 (801.8–1,319.0)	1,059 (606.4–1,713.9)†	784.1 (596.9–1,011.4)‡	636.7 (483.9–837.8)
≥85	1,089.3 (665.4–1,682.4)		2,856.7 (2,469.8–3,287.0)§	1,936.4 (1,431.0–2,620.2)
All	73.6 (69.3–77.9)	108 (85.7–134.1)	76.9 (71.6–82.6)	96.1 (84.6–109.1)
Adjusted world‖	108.2 (95.8–120.6)	137 (112.0–166.4)	105.4 (98.0–113.2)	118.2 (103.1–133.3)

CI, confidence interval; NA, not available.
*These data represent subjects 44 years of age or younger, clustered.
†These data represent subjects 75 years of age or older, clustered.
‡These data represent subjects between 75 and 80 years of age, clustered.
§These data represent subjects 80 years of age or older, clustered.
‖World Health Organization world population.

In Argentina, 2 hospital registries provided data on the most prevalent cardiovascular risk factors in stroke patients. Including 84 centers throughout the country and data from 1,235 patients, the investigators found that the major risk factor was arterial hypertension (78.5%), followed by history of heart disease (34%), smoking (32%), dyslipidemia (31%), previous stroke (22%), diabetes mellitus (17%), and atrial fibrillation (15%) [17]. The second epidemiological registry enrolled 1,991 patients with stroke in 74 public and private hospitals; 83% were ischemic and 17% hemorrhagic events; and the major risk factor was also arterial hypertension (81.6%) [18].

A prevalence study in Cuba showed that the risk profile of stroke patients included history of hypertension (odds ratio [OR]: 2.8; 95% CI: 2.0 to 4.0), low high-density lipoprotein cholesterol (OR: 2.6; 95% CI: 1.7 to 3.9), male sex (OR: 1.7; 95% CI: 1.2 to 2.5), anemia (OR: 1.6; 95% CI: 1.1 to 2.5), history of ischemic heart disease (OR: 1.5; 95% CI: 1.0 to 2.3), carrier of 1 or 2 apolipoprotein E4 genotype (APOE ε4) alleles (OR: 1.4; 95% CI: 1.0 to 2.0), and advanced age (OR: 1.3; 95% CI: 1.1 to 1.9). There was a high prevalence of cardiovascular risk factors with 55.0% of participants reporting a history of hypertension and 18.6% with prior diagnosis of diabetes mellitus [19].

In Brazil, there are some reports with similar results. The formerly mentioned study from a Southern Brazilian city identified arterial hypertension as the most prevalent risk factor among 1,232 stroke cases [17]. Another study retrospectively evaluated consecutive patients diagnosed with ischemic stroke admitted to a tertiary healthcare facility in Brazil and confirmed hypertension as the most frequent risk factor for stroke because it was present in 71% of 421 patients [20].

The CARMELA (Cardiovascular Risk Factor Multiple Evaluation in Latin America) study, a cross-sectional, population-based, observational study in 11,550 adults ages 25 to 64 years evaluated the prevalence of cardiovascular risk factors in 6,119 women according to age and time from menopause. The study was conducted in Barquisimeto (Venezuela), Bogota (Colombia), Buenos Aires (Argentina), Lima (Peru), Mexico City (Mexico), Quito (Ecuador), and Santiago (Chile). The highest prevalence of hypertension and smoking was seen in Barquisimeto, Buenos Aires, and Santiago. The overall prevalence of diabetes mellitus was higher than 7% in Mexico City, Bogota, Quito, and Santiago. Additionally, the prevalence of metabolic syndrome ranged from 12.3% in Buenos Aires to 28% in Mexico City and the prevalence of overweight ranged from 27.5% to 40.8%, with the lowest rate in Buenos Aires [21].

Atrial fibrillation is an important risk factor for stroke and is a major problem in Latin America. Although data regarding its prevalence in Latin America are scarce, it is thought that a large number of people in the region have atrial fibrillation. In Brazil, an estimated 1.5 million patients may be diagnosed with atrial fibrillation [22]. In Venezuela, approximately 230,000 patients may have atrial fibrillation, with this figure predicted to rise to 1 million by 2050 [23].

The contribution of various risk factors to the burden of stroke worldwide is unknown, particularly in low- and middle-income countries, including Latin American countries. Table 3 shows the OR and population-attributable risk of each of the risk factors observed in patients who participated in the INTERSTROKE (Risk Factors for Ischaemic and Intracerebral Haemorrhagic Stroke in 22 Countries) pilot study [24], a case-control study with 3,000 cases and 3,000 control subjects.

TABLE 2. Annual first-ever stroke incidence rates per 100,000 and 30-day fatality by stroke subtype in 4 Latin American population-based studies

	Ischemic			
	Iquique, Chile [9]	Matão, Brazil [12]	Joinville, Brazil [10]	Durango, Mexico [11]
Age, yrs	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Incidence: Total Population, by Age, yrs				
0–24	1.7 (0.3–4.9)	6.8 (0.8–24.6)*	NA	NA
25–34	3.0 (0.4–10.9)		4.6 (2.0–9.1)	2.5 (0.6–10.2)
35–44	11.2 (4.5–23.1)		16.3 (10.5–24.1)	14.8 (8.0–27.6)
45–54	46.3 (28.3–71.5)	151.3 (55.6–329.1)	85.7 (68.5–106.0)	25.9 (14.7–45.6)
55–64	198.5 (145.8–263.9)	639.3 (349.9–1,070.3)	243.9 (202.4–291.4)	82.4 (54.7–129.9)
65–74	361.3 (268.2–476.4)	874.0 (452.4–1,521.7)	441.7 (372.7–519.7)	182.6 (128.4–259.7)
75–84	659.7 (475.5–879.8)	1,393.2 (639.0–2,628.2)†	757.5 (573.7–981.4)‡	424.5 (303.3–594.1)
≥85	762.5 (416.9–1,279.4)		2475.8 (2,116.6–2,878.5)§	1,198.7 (816.2–1,780.6)
All	46.6 (39.8–53.3)	114.6 (82.9–154.3)	61.8 (57.0–66.9)	55.7 (47.2–65.8)
Adjusted world	66.5 (56.9–76.1)	NA	86.0 (79.3–93.1)	69.1 (57.5–80.7)
30-Day Fatality: Total Population				
All ages	17.8 (12.3–25.1)	13.0 (6.1–23.3)	NA	29.0‖

CI, confidence interval; NA, not available.

*These data represent subjects 44 years of age or younger, clustered.

†These data represent subjects 75 years of age or older, clustered.

‡These data represent subjects between 75 and 80 years of age, clustered.

§These data represent subjects 80 years of age or older, clustered.

‖Confidence interval unavailable.

¶Only one 83-year-old patient had subarachnoid hemorrhage in the Matão study.

Latin America coexists with a region-specific risk factor associated with stroke. Chagas disease is considered a public health problem with high mortality and morbidity rates along with substantial disability and associated costs in the region, with approximately 8 million people infected (WHO 2008). Approximately, 30% of infected individuals develop chagasic cardiomyopathy, associated with heart failure, heart block, ventricular arrhythmias, and cardioembolic phenomenon [25]. Stroke had been an unrecognized complication of Chagas disease until recently [26].

A population-based cohort study, with 10 years of follow-up was conducted in Bambuí, a Brazilian southeastern city, to estimate the risk for death from stroke associated with *Trypanosoma cruzi* infection [27] (Table 4). Participants of this study were followed from 1997 to 2007 leading to 9,740 person-years of observation. The baseline prevalence of *T. cruzi* infection was 37.5% and the overall mortality rate from stroke was 4.62 per 1,000 person-years. The risk of death from stroke among *T. cruzi*–infected participants was twice as high as for those who are not infected (adjusted hazard ratio: 2.36; 95% CI: 1.25 to 4.44). Complementarily, this study shows that the B-type natriuretic peptide level in the top quartile was a strong and independent predictor of stroke mortality among those infected (adjusted hazard ratio: 2.72; 95% CI: 1.25 to 5.91). The presence of both, high B-type natriuretic peptide levels and electrocardiographic atrial fibrillation increased the risk of stroke mortality by 11.49 (95% CI: 3.19 to 41.38) in these individuals.

COSTS AND DISABILITY ASSOCIATED WITH STROKE

In addition to its high mortality, patients who survive after a stroke present quite frequently with marked physical limitations and functional disability.

In Junín, Argentina, the community-based study showed that for those who survive after stroke, 52% had moderate to severe disability [16].

In Santiago, Chile, a prospective study of hospitalized patients ages >60 years admitted with an ischemic or hemorrhagic stroke showed that of 122 patients evaluated, 66% had cognitive impairment at 3 months after stroke [28]. After 1 year, 22% of those had dementia, which is double the prevalence expected for persons of the same age in Latin America [29]. The frequencies and independent determinants for dementia (higher functional impairment at hospital discharge, left hemisphere large-vessel–related infarction, large amount of white matter changes) were similar to those found in other cohorts in the United States or Europe [30,31]. Christensen et al. [32] estimated the cost of hospitalization for acute stroke in 2 public hospitals in Brazil. The mean cost of hospitalization was US$1,902 for ischemic stroke and US$4,101 for hemorrhagic stroke. Aggregate national healthcare expenditures for acute treatment of incident hemorrhagic stroke were US$122.4 million and US$326.9 million for ischemic stroke. The investigators emphasized the need for effective prevention and acute treatment to decrease the incidence and the disability and, consequently, reduce the cost [32].

TABLE 2. Continued

Intracerebral hemorrhage				Subarachnoid hemorrhage¶		
Iquique, Chile [9]	Matão, Brazil [12]	Joinville, Brazil [10]	Durango, Mexico [11]	Iquique, Chile [9]	Joinville, Brazil [10]	Durango, Mexico [11]
% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
2.8 (0.9—6.5)	None*	NA	NA	None	NA	NA
1.5 (0.04—8.4)		0.6 (0.01—3.3)	3.8 (1.2—11.8)	1.5 (0.04—8.4)	2.3 (0.6—5.9)	None
8.0 (2.6—18.7)		5.2 (2.2—10.2)	4.5 (1.4—13.8)	1.6 (0.04—8.9)	3.9 (1.4—8.5)	3.0 (0.7—11.9)
32.4 (17.7—54.4)	12.9 (0.3—72.0)	19 .2 (11.6—30.0)	23.7 (13.1—42.8)	13.9 (5.1—30.3)	16.1 (9.2—26.1)	12.9 (5.8—28.8)
84.4 (51.6—130.4)	89.4 (24.4—228.7)	50.4 (32.6—74.1)	43.0 (24.4—76.7)	12.6 (2.6—37)	16.1 (6.9—31.7)	14.3 (5.4—38.2)
57.8 (24.9—113.9)	137.7 (37.5—352.2)	54.8 (32.5—86.6)	64.8 (35.9—117.0)	14.4 (1.7—52.2)	33.5 (16.7—60.0)	23.6 (8.8—62.8)
204.2 (108.7—349.2)	132.4 (16.0—477.3)†	26.6 (3.2—96.0)‡	74.9 (33.7—166.7)	47.1 (3.8—113.5)	39.9 (8.2—116.5)‡	12.5 (1.8—88.6)
163.4 (33.9—477.5)		307.6 (190.4—470.6)§	414.9 (215.9—797.5)	None	102.5 (41.1—211.2)§	138.3 (44.6—428.9)
17.4 (13.5—22)	14.7 (7.3—26.2)	9.5 (7.7—11.6)	22.2 (17.1—26.9)	3.8 (2.1—6.2)	5.6 (4.2—7.3)	8.1 (5.2—12.5)
22.1 (16.9—27.3)		12.9 (10.4—15.8)	26.7 (19.6—33.8)	4.9 (2.4—7.3)	7.0 (5.3—9.1)	9.5 (5.3—13.8)
28.9 (17.7—44.8)	45.4 (16.7—76.2)	NA	48.0‖	40.0 (14.7—87.1)	NA	52.0‖

ACCESS TO ACUTE TREATMENT OF STROKE

It is well established that the primary prevention has an important role in the control of burden of stroke around the world and especially in low- and middle-income countries. On the other hand, it is also known that important aspects of acute stroke care, secondary prevention, and rehabilitation are still largely neglected in these countries [33].

Only a few articles have been published discussing national strategies against stroke in Latin America (Brazil and Chile). Table 5 summarizes stroke systems of care in some Latin American countries (information provided by stroke neurologists in each country).

In a prospective 6-year study of 1,736 consecutive patients with acute ischemic stroke in 3 Brazilian hospitals, 303 patients were treated with reperfusion therapy (238 with intravenous tissue plasminogen activator and 65 with endovascular treatment). Of these 303 patients, 23% were 80 years or older (elderly group). The rate of symptomatic intracranial hemorrhage was 10.9% in elderly patients and 6.6% in nonelderly (p = 0.28), and a substantial

TABLE 3. Significant risk factor for all strokes in the INTERSTROKE pilot study

	Odds Ratio	99% CI	PAR (%)	99% CI
Hypertension	2.64	2.26—3.08	34.6	30.4—39.1
Current smoking	2.09	1.75—2.51	18.9	15.3—23.1
Waist-to-hip ratio*	1.65	1.36—1.99	26.5	18.8—36.0
Diet risk score*	1.35	1.11—1.64	18.8	11.2—29.7
Regular physical activity	0.69	0.53—0.90	28.5	14.5—48.5
Diabetes mellitus	1.36	1.10—1.68	5.0	2.6—9.5
Alcohol intake†	1.51	1.18—1.92	3.8	0.9—14.4
Psychosocial stress	1.30	1.06—1.60	4.6	2.1—9.6
Depression	1.35	1.10—1.66	5.2	2.7—9.8
Cardiac causes	2.38	1.77—3.20	6.7	4.8—9.1
Ratio of apolipoproteins* B to A1	1.89	1.49—2.40	24.9	15.7—37.1

CI, confidence interval; PAR, population-attributable risk.
*Highest versus lowest tertile.
†For more than 30 drinks per month or binge drinking.

TABLE 4. Hazard ratios for 10-year stroke mortality among *Trypanosoma cruzi* seropositive individuals compared with seronegative individuals, the Bambuí cohort study, 1997–2007 [27]

T. cruzi Infection	Deaths/Person-Years at Risk (Death Rate per 1,000), n	HR (95% CI) Adjusted for Age and Sex	HR (95% CI) Adjusted for Age, Sex, Education, and Conventional Risk Factors	HR (95% CI) Adjusted for Age, Sex, Education, and Conventional Risk Factors and C-Reactive Protein Level
Noninfected	20/6,261 (3.19)	1.0	1.0	1.0
Infected	25/3,479 (7.58)	2.28 (1.26–4.12)	2.35 (1.25–4.42)	2.35 (1.25–4.44)

CI, confidence interval; HR, hazard ratio.

proportion of elderly patients achieved a favorable outcome (modified Rankin scale score ≤1) at 90 days, although this proportion was lower than in the nonelderly patients (42% vs. 58%; p = 0.54). Stroke represents a much more frequent problem in the elderly population, which is usually excluded from thrombolytic treatment in some countries. Older patients should not be excluded from treatment, especially in Latin American countries where the burden of the disease also affects the ever-growing elderly population [34]. Medication cost is often 1 of the reasons for not using thrombolytic therapy in stroke patients in low- and middle-income countries. To carry out a cost-effectiveness analysis treatment, the Brazilian Public Health System compared alteplase to conservative treatment. A decision analysis model was developed using the Markov model. In the first year after stroke, the quality adjusted life year gained was 0.06, with an incremental cost of US$1,827 for men and US$1,651 for women. The incremental cost-effectiveness ratio in 1 year was USD 28,956/ quality adjusted life year for men and USD 26,171/ quality adjusted life year for women. After the second year, treatment with alteplase was associated with shorter length of in-hospital stay; lower cost of hospitalization; and a reduction in costs associated with complications from immobility, rehabilitation, and especially on indirect costs, such as lost productivity and absenteeism [35].

Recently, the Brazilian challenges and experiences in the implementation of the National Stroke Project have been reported by Martins et al. [36]. As in other middle-income countries, stroke care follows the social disparities that divide Brazil into "two different countries": the more wealthy part that shares the same profile as developed countries and is able to pay for high-quality

TABLE 5. Stroke systems of care in Latin America

	Population (million)	Type of Health System	Stroke Units	Thrombolytic Therapy	National Guidelines	National Stroke Program
Brazil	193	Public 100% 20% additional private health insurance	3	122 hospitals	Brazilian Stroke Society and Ministry of Health	Yes
Argentina	41	Public 100% 50% additional private insurance	Few private hospitals	Few hospitals	Neurological Society	No
Chile	17	Public 80% 20% additional private insurance	Private hospitals	Private hospitals and 1 public hospital	Ministry of Health	Yes
Costa Rica	0.45	Public 100% 20% additional private insurance	4 2 public 2 private hospitals	4 hospitals	Ministry of Health	No
Mexico	113	Public 100% 3% Additional private insurance	3 hospitals	NA	Ministry of Health	No
Nicaragua	6	Public health 70% 10% workers insurance Private <10%	No	NA	NA	No
Peru	30	Public 100%	3 hospitals	3 hospitals	Peruvian Stroke Society	No

stroke care resources; and the majority of the population that has several limitations to access stroke prevention, acute treatment, and subsequent rehabilitation.

In 2008, a task force including the Brazilian Stroke Network, the Brazilian Stroke Society, the Brazilian Academy of Neurology, the Brazilian Medical Association, the Brazilian Society of Cardiology, and the Brazilian Emergency Network created the National Stroke Project that included 5 main components: 1) educational campaigns; 2) training of emergency medical services; 3) development of stroke centers inside secondary and tertiary hospitals across the country; 4) improvement on prevention of cerebrovascular risk factors in public outpatients' clinics; 5) implementation of programs for early rehabilitation and family support.

A pilot intervention was then planned to provide data for the National Stroke Project in Porto Alegre, a southern city. A pre-hospital team for rescue and transport of stroke patients (SAMU [Serviço de Atendimento Móvel de Urgência]) and 5 stroke centers were trained on acute stroke protocols including thrombolysis. After the pilot intervention, the proportion of stroke patients treated with intravenous thrombolysis increased from 1.7% (65 of 3,824) to 5.3% (206 of 3,860). Moreover, in Porto Alegre stroke centers, the mean thrombolysis rate was 14% (range, 12% to 18%) and after 3 months, 53% (109 of 206) of treated patients had minimal or no disability (modified Rankin scale: 0 to 1), the rate of symptomatic intracranial hemorrhage was 4%, and the mortality rate was 11% [36].

In 2012, 82 stroke centers were active in Brazil (all with thrombolytic therapy), including 45 public hospitals that represent more than the twice the number before the National Stroke Program was devised (Table 6). In April 2012, the Ministry of Health launched the Brazilian Policy for Stroke, including thrombolytic therapy made available to the public hospitals and resources to develop stroke units around the country (Brazilian Ministry of Health Decree 665 of April 12, 2012).

TABLE 6. Structure of the Brazilian stroke system before and after the implementation of the national program

	Before Program (May 2008)	After Program (April 2012)	Increase
Number of states with active stroke center	10	19	1.9×
Number of stroke centers	35	82	2.3×
Private	20	37	1.9×
Public	15	45	3×
Number of stroke units or vascular units	5	17	3.4×

OPPORTUNITIES FOR PREVENTION

Considering that the most common risk factor for stroke in all the countries is arterial hypertension, the screening and treatment for this condition is the main strategy to be pursued for primary stroke prevention. Smoking cessation programs must always be implemented. Physical activity and healthy eating habits are key to prevent hypertension, dyslipidemia, obesity, and diabetes mellitus, and, consequently, stroke rates. Psychosocial factors such as stress and depression could be managed through societal and individual approaches to prevent stroke. Cardiac factors, mainly atrial fibrillation should be detected, and in those patients, effective anticoagulation treatment should be initiated. New oral anticoagulants could be an attractive alternative for better treatment in Latin American countries, where there are difficulties for reaching and maintaining the therapeutic range of anticoagulation with warfarin. Proper etiological investigation after a stroke is also important and should be improved, as there are still a high proportion of patients with stroke who have a history of previous stroke. In summary, targeted interventions that reduce blood pressure and smoking, and that promote physical activity and a healthy diet, have an inherent potential to substantially reduce the burden of stroke.

FUTURE DIRECTIONS

Some countries in Latin America, especially in rural areas, face local difficulties because of the absence of accurate case registries, medical records, and sophisticated technology. Therefore, the methodological approaches used in developed countries are often unsuitable for use in low-income countries. Thus, in some prevalence studies, the door-to-door survey is the only information tool about the burden of stroke available in these areas [15].

Because stroke is the leading cause of death in most Latin American countries and also because it is a clearly preventable cause of death and disability, simple, affordable, and efficient strategies must be urgently implemented in Latin America. Efficient study research designs should be used to fulfill the knowledge gap in the area: 1) to understand risk factors associated with stroke and their clinical impact (case-control and prospective cohort studies); 2) to better recognize demography, presentation, types of stroke, utilized diagnosis tests, implemented treatment, mortality and morbidity rates in-hospital and long-term, and cost-evaluation (cross-sectional studies); 3) to implement into clinical practice evidence-based interventions (knowledge-translation research); and 4) to understand how health systems would influence health outcomes in stroke patients (cluster randomized trials). An efficient Latin American network including collaborative research sites, which could be representative of every Latin American country, should be consolidated by means of simple study protocols focusing on key stroke questions. This strategy would have the benefit of capacity building, new knowledge generation, and population health.

The Brazilian experience with a stroke network linking academic societies and the government constitutes an

example that could be replicated in other countries for early treatment of stroke patients.

Certainly, early recognition and appropriate treatment of stroke from patient and physician perspectives are crucial for reassuring health outcomes for patients, however, in parallel, strategies for primary prevention of stroke are fundamental to substantially reduce the burden of stroke in Latin America. In essence, the burden of disease related to stroke can be substantially reduced by means of the following actions:

1. Taxation of tobacco, restriction of advertising and marketing of these products.
2. Reduction of dietary salt intake by regulation, well-designed public education, and mass media campaigns, as well as incentive of voluntary actions by food manufacturers.
3. Improvement of financial and physical access of population to healthier diets, including fresh fruits and vegetables, healthy fats, and whole grains. Additionally, regulations or restrictions on foods that contain high amounts of sugars, processed carbohydrates, and saturated fats are key for population health.
4. Implementation of universal, financially and physically accessible, high-quality primary care to reduce cardiovascular risk factors through clinical interventions and to enhance early detection and treatment of cardiovascular diseases.

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